Genes, diet and inflammatory bowel disease.

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Abstract

Inflammatory bowel disease (IBD) arises in part from a genetic predisposition, through the inheritance of a number of contributory genetic polymorphisms. These variant forms of genes may be associated with an abnormal response to normal luminal bacteria. A consistent observation across most populations is that any of three polymorphisms of the Caspase-activated recruitment domain (CARD15) gene are more prevalent in IBD patients as compared with unaffected controls. Similar aberrant responses to bacteria are associated with variants in Autophagy-related 16-like 1 (ATG16L1) and human defensin (HBD-2, -3 and -4) genes. The defective bacterial signal in turn leads to an excessive immune response, presenting as chronic gut inflammation in susceptible individuals. Inconsistent population reports implicate the major histocompatibility complex (MHC), that encodes a number of human leukocyte antigens (HLA), MHC class I chain-related gene A (MICA) or cytokines, such as tumour necrosis factor-alpha (TNF-alpha). Toll-like receptors encoded by the TLR4 or TLR9 genes may also play a role. Recent whole genome scans suggest that a rare variant in the interleukin-23 receptor (IL23R) gene may actually protect against IBD. Other implicated genes may affect mucosal cell polarity (Drosophila discs large homologue 5, DLG5) or mucosal transporter function (sodium dependent organic cation transporters, SLC22A4 and SLC22A5). A variant in ABCB1 (ATP-binding cassette subfamily B member 1) may be especially associated with increased risk of UC. While pharmacogenetics is increasingly being used to predict and optimise clinical response to therapy, nutrigenetics may have even greater potential. In many cases, IBD can be controlled through prescribing an elemental diet, which appears to act through modulating cytokine response and changing the gut microbiota. More generally, no single group of dietary items is beneficial or detrimental to all patients, and elimination diets have been used to individualise dietary requirements. However, recognising the nature of the genes involved may suggest a more strategic approach. Pro- or prebiotics will directly influence the microbial flora, while immunonutrition, including omega-3 fatty acids and certain polyphenols, may reduce the symptoms of gut inflammation. The expression of gut transporters may be modulated through various herbal remedies including green tea polyphenols. Such approaches would require that the gene of interest is functioning normally, other than its expression being up or down-regulated. However, new approaches are being developed to overcome the effects of polymorphisms that affect the function of a gene. A combination of human correlation studies with experimental
models could provide a rational strategy for optimising nutrigenetic approaches to IBD.

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